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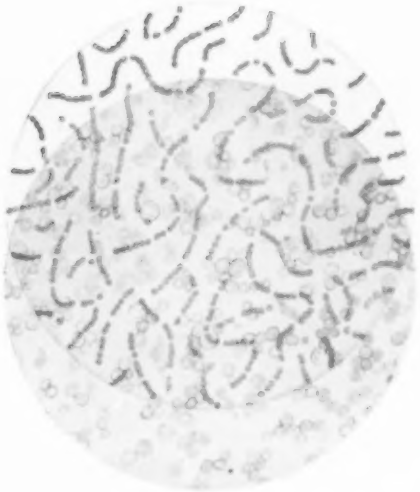

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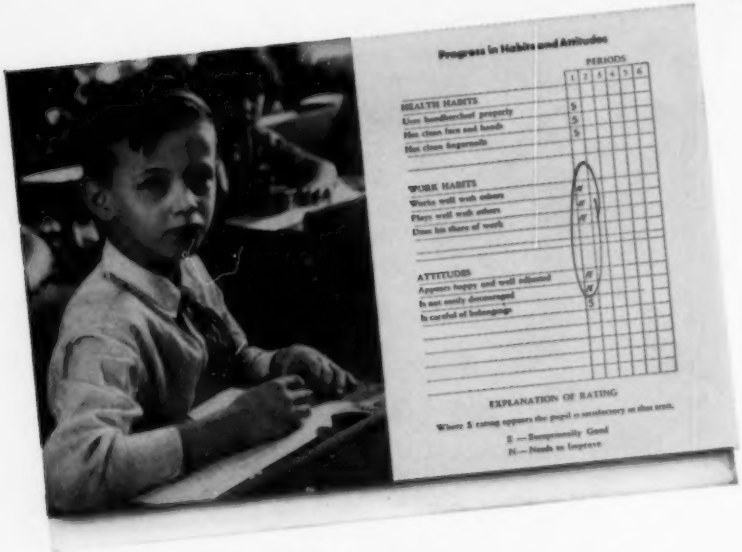

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June 1959
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EYE DISTURBANCES IN INFANCY AND CHILDHOOD

JOSHUA ZUCKERMAN, B.Sc., M.D., C.M., F.A.C.S.*

New York

It is well known that the human eye and its adnexa are unique in many respects. For example, they are connected directly or indirectly with eight of the twelve cranial nerves as well as with the sympathetic nerve.

The eye is equipped with its own highly specialized protective mechanism. Anatomically, the eyeball is protected by the eyebrow, the bony margin of the orbit, the nose, the eyelids with its sensitive cilia, the corneoscleral coat, and by a cushioning pad of retrobulbar fatty tissue. Physiologically, it is protected by head movements, by the closure mechanism of the eyelids, by the sensitivity of the cornea, by the secretion of lysozyme-containing tears, by an efficiently functioning lacrimal drainage system as well as by a light-sensitive mechanism consisting of the iris, pupil, retina and optic nerve.

The important role of the eye in every activity of daily life renders even mild or early derangements noticeable subjectively in contradistinction to disturbances of other organs or of other parts of the body which might go unnoticed, or be disregarded and neglected. The intimate relationship of the eye and its various parts to the rest of the body permits the recognition of many systemic conditions by their manifestations in the eye.

The exposed condition of the eye and its adnexa facilitates examination of the area surrounding the eye, of the margins of the orbit, the eyelids, the cilia, as well as of the cornea, the sclera, the conjunctiva and the lacrimal apparatus. The transparency of the eye allows direct detailed examination of almost all of its structures (the cornea, the anterior chamber with its angle, the iris, the lens, the vit-

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reous and the eyeground). The intrinsic natural magnification of 13x provided by the media of the eye exposes the various parts of the eyeground (the optic disk, the macula with its fovea, the retina, the retinal arteries and veins, and even the choroid) to minute scrutiny. Because of the central vein drains into the cavernous sinus, it reflects evidence of changes in the intracranial circulation.

Since the central artery of the retina is a branch of the interal carotid artery homologous with the cerebral arteries, changes in the retinal arteries generally parallel the changes in the arteries of other parts or organs of the body. The transparency of the retina permits observation of the condition of the capillary bed of the choroid and provides information for drawing many analogies.

Because the optic nerves, the optic chiasm and other parts of the visual pathways (the optic tracts, the optic radiations and the right and left occipital cortex) are so extensive intracranially, they may be affected readily by vascular or bony lesions of various adjacent structures as well as by disease of the paranasal sinuses and by lesions of various parts of the brain extending from the frontal to the occipital areas.

These considerations reflect the informative value of the eye not only as a possible indicator of a general (systemic) or of a remote disease (such as a brain lesion), but also as a barometer of the course of a disease, of its response to treatment and even of its prognosis.

Where can evidence more readily be found of single or of multiple cranial nerve involvement?

Where can such positive indications or suggestions of serious local or general disease be obtained by such simple observations, determinations or tests as, for example, of (a) the visual acuity (optic or 2nd cranial nerve), (b) the ability to elevate the upper eyelid (3rd cranial nerve), (c) the ability to close the eyelids (7th cranial nerve), (d) the sensibility of the cornea (5th cranial nerve), (e) the action of the superior oblique muscle (4th cranial nerve); of the lateral rectus muscle (6th cranial nerve), of all the other extraocular muscles (3rd cranial nerve), and the response of the pupil (3rd cranial nerve) to direct light, to accommodation or to convergence?

Where can evidence be so readily found of paralysis of the sympathetic nerve as manifested by ptosis, miosis and enophthalmos?

Where but in the eyeground can the earliest evidences of local or of general disease be found as manifested by the presence of choked disk, papillitis, cupping or beginning atrophy of the optic

nerve, of exudates, of pigmentary disturbances or by the presence of minute or extensive superficial or deep hemorrhages?

Because the eyes of a child 2 years of age are almost fully developed, eyes of infants and of children are subject to most of the diseases, disturbances and conditions that affect the eyes of adults, in addition to a few particular affections peculiar to the eyes of children and infants.

HISTORY TAKING AND INSPECTION AND EXAMINATION OF THE EYES

The pediatrician expects to encounter certain obstacles or elements of difficulty peculiar to the examination of infants and children. Accustomed as he is in overcoming obstacles, he should have little difficulty in performing an examination of the eyes.

A family history (past and present) of tuberculosis or syphilis, or of illness in the mother, especially during pregnancy, is often informative. A personal history including the details of the type and duration of delivery may be suggestive.

A history of the eye condition must necessarily be elicited either from an overinterested and anxious or from an indifferent parent or guardian, untrained in observation. (In exceptional cases this history, obtained from the parent, is more reliable than a direct history because it is uninfluenced by the subjective feelings of the patient).

Because the pediatrician knows that a child may be easily frightened by a flashlight, by an ophthalmoscope or by more elaborate equipment he generally observes the infant or child casually, preferably from a distance to begin with, until a friendly basis and a proper rapport are established. The examination must then proceed speedily, yet smoothly, and with gentleness, unobtrusiveness tact, sympathy, affection and forebearance.

Much general information can be obtained from inspection and observation by the pediatrician familiar with various conditions associated with congenital deformities of the head. Some of these may present certain characteristic eye signs.

In oxycephaly, for example, the narrow transverse diameter of the head, the shallow orbits and hypertelorism may be associated with nystagmus, strabismus, poor vision, choked disks and optic atrophy. Hydrocephalus and microcephalus may be associated with optic atrophy. A rachitic type of head may be associated with lamellar cataracts.

More specific information can be gained (before the child begins to cry or to struggle) by studying the movement of the eyes and observing the various parts of the eyeballs as they are exposed to view as a result of these movements. In recalcitrant children immobilization ("mummification") of the body and extremities by means of a blanket and the use of an eyelid retractor may be necessary to expose the cornea and other parts of the eye. It may also be necessary to dilate the pupils (by homatropine or neosynephrine) and in certain cases even to administer a general anesthetic to facilitate exploration of the eyegrounds.

Many other obstacles may render examination of the eyes of infants difficult. It is only after a child has reached the age of 3 years, or in some few cases, of slightly less, that subjective responses to simple tests become fairly reliable. Even some of the objective tests, especially the more complex ones, may prove to be inapplicable or unreliable.

So much is expected of the pediatrician! He is expected not only to preach prophylactic care of the eyes in regard to infection or trauma and to point out the advantages of periodic examination of the eyes but also he is expected to be able to detect congenital or acquired defects and to diagnose and even treat some disturbances or diseases of the eyes.

It is he of all specialists who may first notice birth trauma, developmental defects and ophthalmia neonatorum, which account for most cases of blindness in the newborn.

It is he who is generally first consulted concerning eye disturbances that parents notice or suspect in their children. These may include a great number of symptoms and signs, such as photophobia, poor vision, ptosis, red or encrusted eyelid margins, redness of the eyes, tearing, discharge, unusual prominence or recession of one or of both eyes, strabismus (squint) or nystagmus.

Nystagmus of ocular origin is always pendular, that is, the "to and fro" movements are equal. In some cases the sight is fairly good but it is seldom normal. Nystagmus associated with a disturbance of the labyrinth or of the central nervous system presents a rapid and a slow component.

Other etiologic conditions associated with nystagmus are heredity, encephalitis, meningitis, acute cerebellar ataxia, congenital cataract, retrolental fibroplasia, albinism and drugs. Retrolental fibroplasia is a bilateral condition of premature infants of low birth weight, in which the retinopathy is characterized by dilatation of the retinal vessels, retinal exudation, retinal detachment and the formation of a retrolental membrane with resultant blindess.

Some of these conditions may occur or appear to occur during convalescence from a severe general illness that the pediatrician may have been treating.

The pediatrician must be familiar with the appearance and function of the normal eye and be on the lookout for any deviation from normal. He must ask himself, "Are the eyes normal in appearance?" "Are they normal in function?" That the appearance of the eyes is normal can be answered in the affirmative only after a thorough search has been made to exclude congenital or acquired defects.

After having noted the general demeanor, attitude, gait, size and shape of the child's head, the examiner observes the position or posture of the head. Does the patient hold his head so that his face is rotated to the right or to the left? Does he carry his head so that it is tilted toward one shoulder or the other? These abnormal head postures may be adopted to overcome double vision. In the former instance paresis, paralysis or fibrosis of a horizontally acting extraocular muscle may be present; in the latter instance disturbances of a vertically-acting (elevator or depressor) muscle may be present.

The examiner then notes any congenital deformity of the adjacent structures of the eyes and any externally visible congenital abnormalities of the various structures of the eye proper. This is followed by a search for the presence of acquired disturbances.

CONGENITAL ANOMALIES

Congenital Anomalies of Adjacent Structures of the Eye. There are a number of congenital anomalies that involve the adjacent structures of the eye.

Orbit. A cystic mass may be present. When situated at the upper outer margin of the orbit it is generally a dermoid cyst; when situated at the upper inner angle of the orbit and if it becomes more prominent during coughing, crying or straining, it is more likely to be a meningo-encephalocele.

Eyelids. Ptosis of one or of both eyes may be present. (How to diagnose this condition is described under "Function".)

There may be a "V" shaped defect in the eyelid with its base directed toward the margin of the eyelid (coloboma).

The inner angle of the upper and lower eyelids may be partly covered by a vertical, slightly crescentic fold of skin (epicanthus).

Fig. 1 Bilateral epicanthus. A vertical fold of skin juts out on both sides of the dorsum of the nose and partly covers the medial canthus of each eye. When eyes are rotated, one eye becomes partly concealed by the fold of skin so that it appears to be "crossed"

This condition generally disappears as the root of the nose becomes more prominent. Because these folds may give the eyes an appearance of convergent strabismus (pseudo-strabismus) differentiation from true strabismus should be made by observing the position of the eyes when the inner angles are exposed. This may be accomplished by grasping the folds between the thumb and index finger of one hand and drawing them upward and across the bridge of the nose.

If the child is cooperative a much more reliable way to diagnose or to exclude convergent strabismus is by means of the *screen test*, which is described in the section on Strabismus.

Lacrimal Apparatus. In order to be able to detect any congenital defect of the lacrimal apparatus it is important to have a knowledge of its various parts. This apparatus is composed of a tear-producing system consisting of (a) the lacrimal (and the accessory lacrimal) gland situated under the upper outer margin of the orbit and (b) of the tear drainage system (the upper and lower puncta, the canaliculi, the lacrimal sac, and the nasolacrimal duct). The lacrimal puncta may be absent or stenosed. The commonest congenital anomaly of the lacrimal apparatus is obstruction of the lower end of the nasolacrimal duct due to incomplete canalization. This condition which causes persistent unilateral epiphora deserves a more lengthy description. Tearing usually becomes apparent within a few days of life but even normally, tears may be absent during the first few weeks of life. Stasis may result in the development of a mucocele, which in turn may lead to chronic infection with discharge of mucoid or mucopurulent material into the conjunctival sac. In most cases, the condition clears up within the first year of life or can be cleared up by repeated digital compression of the lacrimal sac downward toward the nostril. If tearing is still present by the end of the first year, probing of the nasolacrimal duct is usually necessary.

In some relatively few cases of stasis, an abscess may form (acute dacryocystitis) and a surrounding cellulitis (peridacryocystitis) may occur.

Conjunctiva. The presence of purulent material in the conjunctiva resulting from a congenital anomaly (dacryostenosis) can generally be differentiated from the secretion associated with a

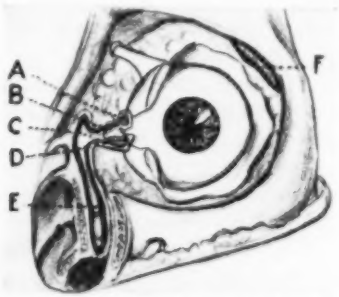

Fig. 2 Lacrimal apparatus of left side (anatomic view). A—upper and lower punctum; B—upper canaliculus; C—lacrimal sac; D—lower canaliculus; E—nasolacrimal duct; F—lacrimal gland

conjunctivitis by the history, unilaterality or bilaterality and by the type of secretion. In the congenital condition, tearing of the affected side usually has set in since, or a few days after, birth; a mucous rather than a mucopurulent discharge is present in the conjunctiva of the affected eye and generally absent in that of the fellow eye; the tear sac may be visibly or palpably distended and mucus may regurgitate at the lacrimal punctum (or puncta) when the tear sac is compressed against its bony bed by the examiner's finger.

CONGENITAL ANOMALIES OF THE EYE PROPER

Among some of the more common *congenital disturbances* of the various structures *of the eye proper* are the following:

Eyeball. An abnormally small eyeball (microphthalmos) is often associated with other abnormalities. An abnormally large eyeball occurs in hydrophthalmos or buphthalmos ((congenital glaucoma).

Conjunctiva. Congenital pigmentation may occur as small, single or multiple moles or as diffuse and irregularly distributed areas (melanosis bulbi). Dermolipomas are usually situated on the temporal side of the eyeball. Teratomas may contain bone or cartilage. Dermoid cysts usually ride the corneoscleral junction. An angioma of the conjunctiva usually extends from an angioma of the eyelid.

Cornea. Microcornea or megalocornea may be present. The surface curvature of the cornea may be abnormally flat or abnormally curved. Transparency is of the utmost importance. Partial loss of transparency may result from a dermoid cyst or from a congenital annular opacity (embryotoxon). A hyaline membrane may be present on the posterior surface of the cornea.

Sclera. Cartilaginous plaques may occur in the sclera. Bluishness (due to thinning of the sclera) may be associated with fragility of the bones and with otosclerosis.

Iris. Absence of the iris (aniridia) often accompanies other developmental anomalies of the eye, such as cataract and persistent hyaloid artery. A defect in the iris tissue (coloboma) is frequently associated with hereditary defects of other parts of the eye. Clumps of pigment in the stroma of the iris usually represent a benign melanoma. A fringe of pigment (flocculus) may occasionally be seen at the margin of the pupil. Persistent strands of pupillary membrane, hyperplasia, hypoplasia and aplasia, are other forms of disturbances of the iris. Lack of pigment in the iris (resulting in translucency) is often part of the entire picture of lack of pigment in the skin and in other parts of the body (albinism).

ACQUIRED DISTURBANCES OR CONDITIONS OF THE EYE AND ITS ADNEXA

After having detected or excluded the presence of congenital disturbances of the adnexia of the eye and of the eye proper, it is important to determine whether there are any *acquired disturbances or conditions* of the various parts of the *adnexa of the eye and of the eye proper.*

Eyebrow. The eyebrow may be abnormally elevated, the hairline may be discontinuous; there may be sparsity, absence or discoloration of the hair, seborrhea, acne, furuncles or insect bites.

Margin of Orbit. Both orbits may not be on the same horizontal plane. There may be a mass, redness, swelling, depression, fistula, scar, unevenness, alteration in the shape of the margin of the orbit or crepitus.

Orbit. Inflammation, orbital cellulitis, solid, cystic or vascular tumor or pseudotumor, hemorrhage, emphysema or fracture of the orbit may be present.

Eyelids. The eyelids may present disturbances of their position as a whole or only of their margins.

The upper or lower eyelid may be elevated or depressed. Nor-

mally when the gaze is directed straight ahead, the margin of the upper eyelid should cover about 2 mm. of the upper part of the cornea and the margin of the lower eyelid should lie just at the lower limbus. Marked variations are usually pathologic.

The eyelid margins may be adherent (ankyloblepharon), or they may either turn in toward the eyeball (entropion), or turn out, that is, away from the eyeball (ectropion), in spastic, cicatricial, paralytic or senile conditions.

The skin of the eyelids may present: ecchymosis in scurvy and whooping cough and in localized trauma; edema in measles, trichinosis and in localized lesions such as styes, insect bites, orbital cellulitis or ethmoiditis; eruption in the exanthemas; chalazions, cysts, xanthelasma, molluscum, warts, cutaneous horns, scars and vascular and nonvascular tumors. (See Table I.) The margin of the eyelids may present redness, thickening, crusts, blebs, excessive meibomian secretion or new growths.

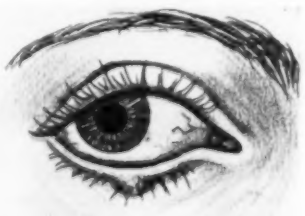

Fig. 3 Hordeolum externum (stye). Hair follicle infection involving one or several cilia of lower eyelid

Cilia. The cilia may be abnormally abundant, scanty, absent, misdirected, discolored, pediculous, crusted (in blepharitis and in blepharoconjunctivitis), matted together (in conjunctivitis), or one may be infected at the root (hordeolum).

Meibomian glands. The orifices of the meibomian glands lie posterior to the follicles of the cilia. The glands may present evidence of acute or chronic inflammation (chalazion), excessive secretion (meibomianitis), growth, blebs, suppuration, concretions or infarcts. The pediatrician is often required to differentiate between an hordeolum and a chalazion (See Table 1).

Conjunctiva (and semilunar fold). The conjunctiva may present foreign bodies, concretions, infarcts, ulcerations, lacerations, erosions, chalazia, granulomas, roughness, hyperemia, pallor, jaundice, inflammations (conjunctivitis— catarrhal, membranous, pur-

ulent, trachomatous, viral, allergic, phlyctenular, vernal, parasitic, dermatologic, etc.), follicles, excessive dryness, excessive moistness, mucoid, mucopurulent, fibropurulent or purulent discharge, evidence of burns, of symblepharon, xerosis or chemosis, emphysema, subconjunctival hemorrhages, pigmentation, cysts, or tumors, (papillomas, adenomas, epitheliomas, fibromas, lymphomas, lymphosarcomas, nevi, melanomas.)

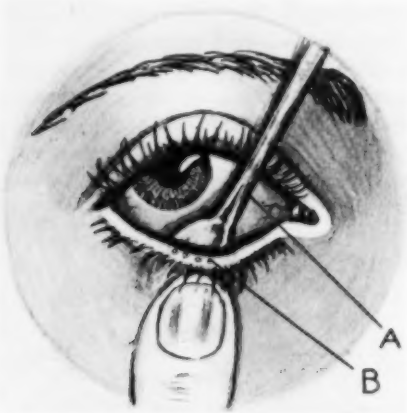

Fig. 4 Location and method of expression of meibomian glands. A—spatula; B—secretion expressed from orifices of meibomian glands

Caruncle. This area of modified skin situated on the semilunar fold of the conjunctiva may appear sunken (following injury or a surgical procedure on the medial rectus muscle), inflamed or hypertrophied, and may bear benign or malignant, pigmented or nonpigmented growths and maldirected, or unusually long, hairs which may cause irritation of the eye.

The Lacrimal Apparatus. The various parts of the secreting and drainage system have been described previously in the section on congenital anomalies of adjacent structures of the eye.

Secretion of lacrimal fluid may be excessive or insufficient. The lacrimal glands may be enlarged as a result of inflammation (in mumps—dacryoadenitis), tumor or dacryops (cystoid dilatation). In order that the lacrimal drainage system of each eye may function properly, the punctum, the canaliculus, the tear sac and the nasolacrimal duct must be patent. The puncta must be in their proper position pointing into the lacrimal lake and the passages must

be unoccluded and unobstructed by inflamed mucous membrane, foreign body, eyelash, Streptothrix, Leptothrix, or purulent, bony or neoplastic material.

Acute or chronic dacryocystitis or a prelacrimal abscess may be present.

Eyeball. The following should be noted:

(1) The anteroposterior position of the eyeball. Is exophthalmos (protrusion or proptosis) or enophthalmos (a sunken appearance) present?

Fig. 5 Chalazion presenting on conjunctival surface of upper eyelid

(2) Congestion. Is it conjunctival (associated with superficial inflammations) or ciliary (associated with deep inflammations) of the eye? (See Table II).

(3) Pigmentation. The eyeball may be yellow in jaundice, brownish in argyrosis, red followed by brown or yellow in subconjunctival hemorrhage and bluish in fragilitas ossium.

(4) Size. Is the eyeball larger than normal as in megalophthalmos, buphthalmos or hydrophthalmos (infantile glaucoma)? Or is is smaller than normal as in microphthalmos?

(5) Tension. Is the intraocular pressure normal, higher or lower than normal? The tension can be estimated roughly by palpation through the upper eyelid, above the tarsus, with the tip of the index finger of each hand placed side by side, while the patient looks down. Pressure is exerted against the eyball with one finger while the eyeball is kept steady with the other. Hardness (glaucoma) or softness is estimated by the sense of fluctuation transmit-

TABLE 1

Differential Diagnosis: Hordeolum Internum, Hoedeolum Externum and Chalazion

	Hordeolum Externum	Hordeolum Internum	Chalazion
Pain	Present	Intense	Only discomfort
Edema	Of eyelid with pointing externally	Marked pointing on conjunctival surface	Localized swelling and "cyst" formation
Redness	Of eyelid	Of eyelid—yellowish spot in conjunctiva of tarsus	Localized grayish-red area in conjunctiva of tarsus
Tenderness	Marked and localized	Marked and localized	Absent or slight
Location of lesion	In Zeis's gland—on anterior margin of eyelid.	In a meibomian gland—behind anterior margin of eyelid	In a meibomian gland—behind anterior margin of eyelid
Course of lesion	Acute—may rupture or subside	Yellow spot seen in tarsus through tarsal conjunctiva; may rupture through conjunctival surface or empty through natural orifice, seldom through skin	May be chronic or subacute. May rupture through conjunctiva
Secretion	None—but after pointing, thick pus may appear	None—but may appear on conjunctival surface after rupture or at natural orifice on edge of eyelid when expressed	None, unless breaks through, then liquefied contents may exude

ted to the stationary finger and the amount of pressure necessary to dimple or to indent the sclera. Estimation of the tension in this way is often misleading; instrumental measurement (by means of a tonometer) is accurate but difficult to perform in children.

Cornea. The most important requisite for the cornea is the maintenance of transparency. The size, shape and curvature of the cornea should be noted. Keratoconus is a central noninflammatory conical bulging or protrusion; keratoglobus is associated with buphthalmos or hydrophthalmos.

Careful examination should be made for the presence of foreign bodies, haziness, dullness, unevenness, abrasions, erosions, ulcerations, vesicles, filaments, bullae, dessication, exfoliation, infiltrations, vascularization, phlyctenules, dystrophy, keratitis, and for keratic precipitates and fibrinous or plastic exudates on the posterior surface of the cornea.

Sclera. Not only the normally visible interpalpebral part of the sclera but also the other parts of the sclera exposed by separating the patient's eyelids should be inspected to note the color (yellow in jaundice), and the presence of congestion or nodules (episcleritis, scleritis), of bulging (staphyloma or ectasia), of ulcerations, cysts or ruptures.

Anterior chamber. The aqueous-filled area between the posterior surface of the cornea and the anterior surface of the iris is the anterior chamber. Is it deep or shallow? Are its contents abnormal? If so, does it contain blood, cysts, fibrin, precipitates, pus, strands of vitreous, hairs, cotton, or any foreign body?

Iris. It is important to note the color, loss of iris markings, congestion, atrophy, tears, synechiae, pupillary membrane, iridodonesis (tremor of the iris) iridodialysis (separation of the iris from its root, nodules, tumors, cysts, coloboma (defect in the iris), or aniridia (absence of the iris).

Pupil. The examiner should note whether there is only one or more than one opening present in each iris as well as the position of the pupils, their shape and size and whether both pupils are equal. (The pupillary responses are described under "Function.")

Lens. It is important to look especially for loss of transparency—(cataract). It should also be noted whether there is any pigment or adhesion to the capsule of the lens and whether the lens is subluxated, dislocated or absent (aphakia). Cataracts may be associated with German measles, toxoplasmosis and galactosemia. An ectopic lens is the most constant finding in Marfan's syndrome.

Certain Eye Disturbances Associated with Systemic Conditions. Additional eye disturbances associated with systemic conditions may be grouped under the following captions:

Nervous diseases: Cerebromacular degeneration, demyelinating diseases, fibromatosis (associated with congenital glaucoma), meningitis, encephalitis, brain tumors or brain abscess. Syndromes associated with pupillary disturbances are rare in children.

Nutritional disturbances: Vitamin deficiencies.

TABLE 2

Differential diagnosis: Conjunctival and Ciliary Congestion*

Symptoms and signs	Conjunctival or superficial congestion	Ciliary or deep congestion
Pain	Usually absent	Usually present
Photophobia	Usually absent	Usually marked
Color of the congested area	Brick red	Purplish or pink
Location	More marked in fornices and in the tarsal conjunctiva	More intense circumcorneally
Course of vessels	Irregular and tortuous	Straight; radiating from cornea
Mobility of vessels	Can be moved with the conjunctiva	Cannot be moved by traction on the conjunctiva
Blanching		
by vasoconstrictors	Blanched	Not blanched
by pressure	Not blanched. Vessels anastomose freely so that vessels emptied by pressure refill at once	Blanched for a second or two after pressure with eyelid or with glass spatula against the eyeball
Discharge	Pathognomonic when present (but may be absent)	Absent
Pupil	Unaffected	Usually contracted
Iris	Unaffected	Usually contracted
Tenderness (near cornea)	Usually absent	Usually present

* Table modified from Berens and Zuckerman "Diagnostic Examination of the Eye", Philadelphia, Pa., J. B. Lippincott Co., 1946.

Metabolic-endocrine disturbances: Diabetes, hyperthryoidism and hypoparathyroidism.

Blood dyscrasias: Leukemia, anemia, as well as other blood affections should be borne in mind.

Lesions generally related to tuberculosis: Phlyctenular conjunctivitis, Coat's disease and nodules in the sclera and iris.

Allergic conditions: Of the eyelids (urticaria, angioneurotic edema, and contact dermatitis; of the conjunctiva (conjunctivitis, dermatoconjunctivitis, vernal catarrh); of the cornea (phlyctenular, interstitial, marginal, and disciform keratitis, contact and atopic reactions), and allergies of the sclera (atopic and microbial).

Psychosomatic and psychogenic factors should also be considered.

Trauma. Because a child with an eye injury is often first seen by the pediatrician he may find that it is incumbent upon him to know how to manage the condition, to evaluate the extent of damage, and to decide whether referrel to an ophthalmologist is necessary.

The pediatrician can take care of simple lacerations of the eyelids, corneal abrasions and foreign bodies of the cornea and conjunctiva but he should refer more serious injuries, such as contusions, deeply imbedded foreign bodies and perforating injuries to an ophthalmologist.

In using fluorescein solution for the detection of denuded areas of the cornea, it is important to bear in mind that the solution may be contaminated by Pseudomonas organisms which may destroy the eye. It is also worthwhile remembering that repeated instillations of anesthetic solutions may interfere with the healing of the corneal epithelium.

Chemical burns, especially alkalis (ammonia or lye), should be immediately and profusely flushed out of the eye with water and then referred to an eye specialist.

Subconjunctival hemorrhages resulting from trauma absorb rapidly and spontaneously but bleeding into the anterior chamber may result in secondary glaucoma.

All perforating injuries should be referred to an ophthalmologist.

FUNCTION OF THE EYES AND THEIR ADNEXA

After having excluded or detected the presence of congenital or acquired disturbances of the adnexa and of the eye proper, it is important to determine whether *the eyes and their adnexia function* normally.

Function may be considered from various aspects, for example, (1) the ability to open or close the eyelids, (2) the pupillary reactions, and (3) the vision, refraction, motility, and muscle balance.

(1) *The Ability to Open or Close the Eyelids.* The patient may be unable to open the eye (actually unable to elevate the upper eyelid—ptosis); or to close the eyelids (paralysis of the orbicularis muscle) of one or of both eyes.

The upper eyelid may actually droop (ptosis) or only appear to droop (pseudoptosis). Differential diagnosis between true and false ptosis may be made by immobilization of the frontalis muscle on the same side by pressure with the examiner's hand applied above the patient's eyebrow while the child attempts to look upward at an object, held upward for that purpose. If the upper eyelid can be elevated (when the frontalis muscle is immobilized by this maneuver), ptosis is absent. If it cannot be elevated, ptosis is present.

That the eyelids can be closed, is readily determined by its response to a suddenly approached object or by touching the cornea with a moistened wisp of cotton.

In the newborn, eyelid closure reflexes, that is, contraction of the orbicularis muscle can be elicited by flashing a bright light at the eye.

The presence of abnormal movements of the eyelids, such as spasm, twitching, infrequent blinking, and the presence of associated eyelid movements, such as "pterygoid" or "jaw-winking" and "medial rectus winking", should be noted.

(2) *The Pupillary reactions.* It is important to test the pupillary reactions not only for their value as evidence of the presence of sight in the infant and for the detection of local disturbances but also in some instances, for the diagnosis of abnormal conditions of the central nervous system.

The direct light reaction is tested while the patient looks off into the distance. A light is directed at the pupil while it is noted whether contraction occurs. Contraction (and dilatation) of the pupil should occur simultaneously and to the same degree in each eye.

In the normal consensual reaction, light directed at the pupil of one eye results in contraction of the pupil of the other eye and vice-versa.

In the normal accommodation-convergence reaction, the pupils contract when a nearby object is observed.

The cervical sympathetic nerve dilates the pupil. In paralysis of the sympathetic, instillation of cocaine solution will not produce dilatation of the pupil.

(3) *Vision.* "Is vision present? Is it good, fair or poor?" are common questions, parents expect the pediatrician to answer. "Is the fair or poor vision due to an error or refraction? do the eyes fixate properly, can they be rotated into the cardinal directions of gaze? is strabismus or nystagmus present?" are some of the questions the pediatrician must ask himself.

The absence of fixation and the vacant stare of the newborn are due to the absence of postural, auditory and tactile experiences and to the fact that the visual pathways and the fovea are not completely developed until several months after birth.

After the first few weeks of life a valid impression of an infant's ability to see can generally be obtained by noting whether he responds to light or to bright colors and whether he follows a light into various directions or responds to friendly gestures. At this age a vacant stare or lack of expression may be suggestive of defective vision, optic atrophy or mental deficiency.

At 3 months of age, a rough idea of the vision may be obtained by noting whether the infant is alert and curious or unaware and indifferent. He should be attracted to toys and should be able to recognize his mother or his milk bottle and his eye movements should have become coordinated.

Normally, a red pupillary reflex can be elicited quite readily with the lens-carrying disk of the ophthalmoscope rotated to plus 6.00 and held approximately 6 inches from the infant's eye. If a red reflex is visible, the cornea, lens and vitreous may be assumed to be clear. If a red reflex is absent, the cornea may be opaque (scarred), the lens may be opaque (cataract), or the vitreous may be hazy or dense (hemorrhage, abscess, tumor, retinal detachment).

The more experienced examiner may be able to obtain a view of the *fundus* and its details.

In examining the *optic disk*, he may note: (1) Papilledema. This is present in 90 per cent of children with space-occupying intracranial lesions. In the very young with unfused cranial sutures, papilledema may be absent until late. (2) Optic atrophy. In children pallor of the optic disk is not a reliable criterion for the diagnosis of atrophy. Optic atrophy may occur in tuberous sclerosis, toxoplasmosis, Schüller-Christian disease, craniostenosis, glioma of the optic chiasm, and in poisonings.

In examining the *retina*, he may note: (1) Retinal hemorrhages. These are common in the newborn. Hemorrhages occurring later

may indicate the presence of a subdural hematoma. (2) A cherry red spot at the macula. This is found in Tay-Sach's disease and in Niemann-Pick's disease. (3) Nodules, mulberry-like masses or oval gray flat areas. These occur in tuberous sclerosis and are associated with mental retardation and telangiectasis. (4) Vascular formations. Angiomatosis may affect the retina alone (von Hippel's disease) or both the retina and cerebellum (Lindau von Hippel's disease).

If the child is old enough (or intelligent enough) to be communicative, his (a) *central vision* can be determined readily by the use of the standard Snellen visual acuity "E" chart (Fig. 6) placed 20 feet away.

Fig. 6 Illiterate "E" chart for testing vision in children

If the direction of the "E" on the topmost line is identified the vision is 20/200; if the directions of E's on the second line are identified vision is 20/100; successive lines represent 20/70, 20/50, 20/40, 20/30 and 20/20.

(b) *Peripheral vision* can be determined by the confrontation test in which the examiner faces the patient and compares his field of vision with that of the patient.* This test may be performed

* "Perimetry" by Joshua Zuckerman, Philadelphia, Pa. J. B. Lippincott Co., 1954.

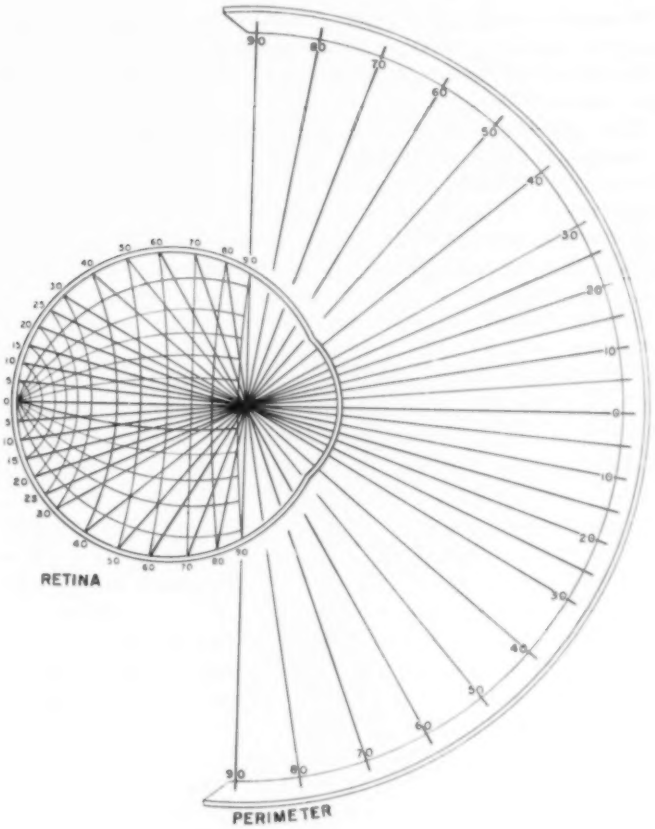

Fig. 7 Peripheral field of vision as projected on a curved surface

binocularly or monocularly. The examiner faces the patient at a distance of about a yard so that both pairs of eyes are level with, are directly opposite to, and fix each other. In the monocular test the eye that is opposite the patient's covered eye is covered. The patient's exposed eye fixes the examiner's exposed eye so that a field of vision common to both is situated in a plane midway between them.

If the patient's vision is not markedly reduced, a small white sphere or a small white disk may be employed as a test object. If visual acuity is poor a larger white test object (from 10 to 20 mm.)

or even the examiner's fingers, his hand or even a small light may be substituted as a test object. It is important to ascertain that the test object is as nearly midway as possible between the patient and the examiner.

The confrontation test is used for examination of the following specific parts of the field of vision: (A) the fixation area, for the detection or exclusion of a central scotoma; (B) the blindspot, for enlargement or extension; (C) the peripheral outline or isopter, for the detection of gross general contractions; (D) the entire area within the periphery for the detection of peripheral or intermediate scotomas.

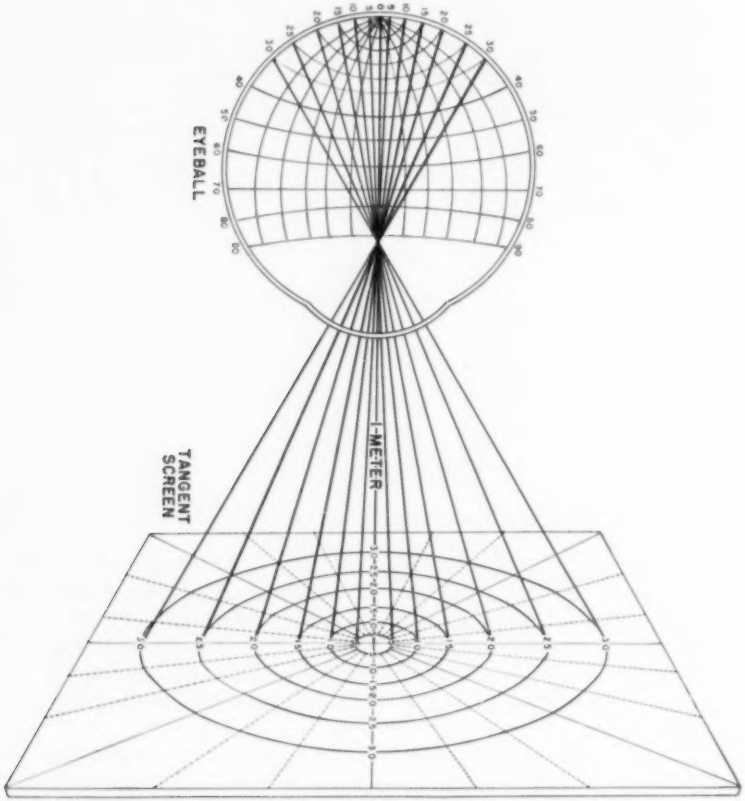

Fig. 8 Central field of vision as projected on a flat surface

(4) *Refraction.* In children, *errors of refraction,* especially when mild in character, may result in headaches or in pain due to sustained contraction of the ciliary muscle or in pain referred to the area of distribution of the fifth cranial nerve, resulting in hyperesthesia, or even occasionally in vomiting due to vestibular upset, and in general physical or mental disturbances. When the error of refraction is of high power, the patient makes little or no attempt to improve his vision but when it is of low power, he attempts to do so by means of the ciliary muscle (accommodation). As this effort is continually exerted, the strain oversteps the patient's limit of muscular capacity, and distress results analogous to the pain or discomfort that accompanies overtaxation of the heart muscle beyond its limits. In other words, it is the continuous effort exerted in an attempt to correct the error of refraction rather than the error of refraction itself that produces symptoms.

Like the heart muscle, the ciliary muscle, used in focusing, and the medial rectus muscles used in convergence, must maintain a physiologic reserve of power.

Many symptoms of visual defects, erroneously attributed to straight-forward errors of refraction may in reality constitute evidence of early signs of disease of the eye or of the general condition of the patient.

A high degree of myopia may give a false impression of the presence of convergent squint. In this condition the visual axis (an imaginary line extending from the fovea to the optical center of the cornea) may be directed normally to the temporal side of, instead of directly through, the geometric center of the cornea, so that a convergent squint (crossed eyes) is simulated. In high hypermetropia on the contrary the visual axis is directed normally to the nasal side of the center of the cornea so that a divergent squint (wall eyes) is simulated.

Symptoms of eyestrain may occur in a feeble, ill or anemic child even in the absence of an error of refraction. Progressive myopia in rapidly growing children, especially girls approaching puberty, requires accurate correction of the error of refraction and may be helped by adequate diet, endocrine therapy and restriction of certain activities.

Headaches and eyestrain may also occur, even in the absence of an error of refraction, in a school child unprepared or unfit to handle the strain of life, or in a child, who attempts to undertake more than he is capable of handling mentally or physically.

(5) *Strabismus.* Strabismus (squint) is a fairly common occurrence in children. Its early detection is important not only for esthetic reasons but also to avoid the development of amblyopia (blunt vision) in the deviating eye and to maintain, develop or restore binocular vision.

A fair impression of whether the eyes are "straight" and whether they move together as a team can generally be obtained by noting whether the reflection of a light directed at the eye falls on corresponding parts of the cornea of each eye.

During the first few weeks of life, a transient strabismus or deviation of either eye is seldom of significance. It may be considered as part of the oscillatory movements which precede the development of steady binocular fixation. Binocular fixation (of a light) cannot be attempted before the age of 6 weeks and cannot be maintained until the age of 5 or 6 months. Rhythmic oscillation of one or of both eyes, however, may indicate a disturbance of the eyes proper, or suggest the presence of a lesion in the labyrinth or in the posterior fossa.

As indicated previously, a slight convergent strabismus may normally appear to be present in epicanthus and in high myopia and a slight divergent strabismus may normally appear to be present in high hyperopia. To rule out or diagnose the presence of a true strabismus, the screen test should be performed. In this procedure a card or screen is held in front of one eye of the child while he is directed to fix with the other eye a small light held at 25 cm. The screen is then quickly shifted to the other eye and the direction of the movement of the abruptly uncovered eye is observed as it attempts to fix the light. If it moves outward (temporally) to fix the light (it must have been directed inward, that is, nasally, behind the screen, then either esophoria (that is, a latent cross-eyed condition) or esotropia (that is, an actual manifest cross-eyed condition) is present. This test should be repeated by covering first one eye then the other in order to make sure that the findings are consistent. The tests should also be repeated while the patient fixes an object in the distance (6 M.).

The history of onset of the squint may also be unreliable. A strabismus which may have been present since birth may be reported as having appeared much later, e.g., at the age of 2 years (or later) or vice versa. In the former instance a fibrotic or a paralyzed muscle is generally present; in the latter, a concomitant squint is usually present. As a rule concomitant strabismus sets in between the ages of two and six years when the child begins to

direct his eyes more continuously at near objects and the squint is much more commonly convergent than divergent. Convergent strabismus is usually associated with hypermetropia (farsightedness); and divergent strabismus with nearsightedness (myopia) in one or in both eyes.

Moreover, certain tests may lead to wrong conclusions. For example, erroneous diagnosis may result in cases in which reliance is placed on tests which presuppose the presence of good vision in both eyes although one eye may have insufficient (or no) vision to participate in these tests.

Furthermore, in some early cases of latent strabismus the eyes may appear straight (orthophoric) during the performance of the tests, misleading the examiner to conclude that strabismus is absent although actual deviation of the eyes does occur when the child is tired or upset.

(6) *Mobility.* Squint cases should be investigated clinically in the following manner: After the visual acuity for each eye separately has been determined, precisely with the "E" chart, or only roughly, with various characters or objects depending on the age and intelligence of the child, a careful inspection is made of the movements and of the direction of the eyes.

First, the *conjunctive movements* are observed as the eyes are spontaneously carried into the various fields of gaze and any derangements of these movements, such as conjugate paralysis or conjugate spasm of the associated movements, are noted. Then any tremor or ataxia of the associated movements, such as searching movements, nystagmus or pseudonystagmus, or any absence of the associated movements (dissociation of the eyes) is noted.

While observing the movements of the eyes it may be observed that (a) the eyes deviate abnormally—the deviation of the eyes may be horizontal, vertical or torsional. In a horizontal deviation the eyes may be convergent (esotropia) or divergent (exotropia); in a vertical deviation one eye is higher than the other (hypertropia); in a torsional deviation the vertical axis of one or of both eyes is rotated away from the perpendicular; (b) their movements are limited—in certain positions of the eyes one eye may fail to follow the other due to paralysis or to congenital fibrosis of an extraocular muscle and not simply as an anomaly of convergence, of divergence or of supravergence, or (c) the movement of the eyes is excessive in certain positions of the eye—one eye may overshoot or move ahead of the other (spasm of an extraocular muscle).

(7) *Orthophoria and Heterophoria.* Normally, the eyes act in conjunction—when one eye fixes an object with its fovea, the other eye also fixes with its fovea (binocular fixation). This condition is called orthophoria when it is maintained normally whether both eyes are exposed or one is covered.

In some cases, both eyes fix the same object only when both eyes are exposed. When either eye is covered, the covered eye deviates while the other (the uncovered) eye continues to fix the object (heterophoria). In other cases, when both open eyes are uncovered, only one eye is directed at the object which is being fixed while the other deviates (heterotropia, strabismus or squint). In either heterophoria or heterotropia the eye may deviate temporally, nasally, upward or downward. Combinations of deviations are common.

If the child can cooperate, the *voluntary* or command *excursion test* is used to ascertain whether each individual extraocular muscle can function properly. The patient is directed to look successively (with his head steady and upright) in the six cardinal directions of gaze, namely, eyes right; eyes left; eyes right and upward; eyes right and downward; eyes left and upward; eyes left and downward.

In the *monocular fixation excursion test* one eye is occluded while the patient fixes with the other eye a small light, which is carried in the six cardinal directions of gaze. It is noted whether the fixing eye follows steadily and uniformly, or fails partly or completely to follow the test object in any of these directions. Limitation may result from paresis, paralysis, fibrosis, or adhesions, following tenotomy or excessive recession or retroplacement of an extraocular muscle.

The *binocular excursion test* is performed in the same manner as in testing monocular fixation excursion, but the patient is directed to fix the test object with both eyes. It is noted not only whether one eye follows uniformly or lags (paresis or paralysis) but also whether the other eye follows steadily, lags behind (paresis or paralysis), or shoots ahead (spasm) of the first eye.

The possibility that an extraocular muscle anomaly may be congenital should always be kept in mind. Some patients with congenital anomalies fix with the paretic eye, others with the nonparetic eye. As previously pointed out, postural abnormalities and head tilting and turning depend on the muscle or muscles involved and whether the paretic or nonparetic eye is the fixing eye. Diplopia

is often overcome by head tilting unless the vision of one eye is suppressed, in which case head tilting is unnecessary.

Special attention should be directed to the possible presence of a retraction syndrome characterized by a complete or partial absence of abduction (lateral rectus muscle) of the affected eye, retraction of the eyeball and narrowing of the palpebral fissure in adduction (and an oblique movement of the affected eye upward and nasally, or downward and nasally upon adduction). Retraction results from the presence of an inelastic fibrous band instead of a (lateral rectus) muscle. (Less commonly fibrosis of the medial rectus may be present.)

A latent or slight deviation which may be overlooked by inspection and by the relative positions of a light reflected on the two corneas, may readily be detected by the cover and uncover test. This test is performed while the child fixes a light at a distance of 6 M. and then repeated while fixing a light at 25 cm. While the light is fixed, a card is deliberately shifted from one eye to the other, so that during the test either one eye or the other is always covered and the uncovered eye always fixes. It is observed whether either eye as it is being uncovered, remains stationary or moves to fix the light. If neither eye moves to fix the light when the card is removed (that is, neither eye deviates under cover), orthophoria (normal muscle balance) is present. If each eye moves into the fixing position when uncovered (that is, it deviated when covered), heterophoria (faulty muscle balance) is present.

In heterophoria the eye behind the screen may be directed outward, inward, downward, or upward (that is, exophoria, esophoria, hyperphoria or hypophoria, respectively, may be present). Whether the deviation is latent (heterophoria) or manifest (heterotropia) can best be determined by the ophthalmologist.

The position of the image of a bright light on the cornea may be of value in checking fixation, in diagnosing some motor anomalies and in estimating the amount of deviation present in a case of strabismus. To measure the deviation, the reflection of the light is centered on the cornea of one eye while the position of the image on the other eye is noted. If it is off center, each millimeter of displacement from the center of the cornea represents approximately 8 degrees of arc. For example, if the reflection is decentered 3 mm., a deviation of approximately $8 \times 3 = 24$ degrees of arc is present.

SUMMARY

The pediatrician is often the first consulted concerning a child's

poor vision. He may also be responsible for diagnosing developmental defects, birth trauma and ophthalmia neonatorum.

It is of utmost importance to obtain an adequate history of the child's difficulty, to inspect the eyes and their movements, and to perform as thorough an eye examination as possible.

The more common congenital and acquired ophthalmologic conditions are enumerated and described. The part the pediatrician is called upon to play is stressed, not only in recognizing and interpreting their local significance but also in interpreting them as suggestive of more remote or systemic conditions.

Data are presented on the differential diagnosis between conjunctivitis and dacryostenosis, between true ptosis and pseudoptosis, between hordeolum internum, hordeolum externum and chalazion, between conjunctival (superficial) and ciliary (deep) congestion and between strabismus and pseudostrabismus. Information on the management of eye injuries by the pediatrician, the value of the confrontation test, the clinical method for detecting tension and a rapid method for estimating the amount of deviation of the eyes in degrees is also provided. Illustrations of the anatomy of the lacrimal passages and of the field of vision as it is represented in the retina are included.

Function is considered from various aspects, namely, the ability to open or close the eyelids, pupillary reactions, vision, refraction, strabismus, motility, orthophoria, and heterophoria.

Thorough routine ophthalmologic examination is recommended so that early treatment can be instituted to prevent further damage and/or to preserve vision.

Figs. 1 to 5 taken from "Diagnostic Examination of the Eye," Berens, C. and Joshua Zuckerman, Phila., Pa., J. B. Lippincott Co. 1946
Figs. 6 to 8 taken from "Perimetry" or "The Field of Vision," Joshua Zuckerman, Phila., Pa., J. B. Lippincott Co. 1954

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ISONIAZID IN A PROBABLE ROLE IN TUBERCULOSIS CONTROL*

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In our fight against tuberculosis, as in other infectious diseases, we must rely mainly on preventive measures. Our first objective must, of course, be to prevent infection, by eliminating exposure of individuals to the tubercle bacillus and when infection has occurred, as shown by a positive reaction to tuberculin, we must try to prevent the tuberculous infection from developing into tuberculous disease.

Since it is estimated that there are approximately 150,000 cases of open tuberculosis in the U.S.A., unknown to the authorities, it is obvious that we can accomplish very little by relying on isolation of these cases. Before these individuals are diagnosed, and properly isolated, vast numbers of contacts have unknowningly become infected and these in turn, become in due course of time, new foci for the further spread of the disease.

Our efforts, up to very recent years, to prevent tuberculous infection from developing into tuberculous disease, have been equally inadequate. Once infection with the tubercle bacillus has taken place, as shown by a positive tuberculin reaction, there was nothing specific to do to prevent the development of serious complications. While the risk is less in favorable circumstances, we must remember that it is never negligible and never predictable. When a serious complication, such as, tuberculous meningitis did develop, it was almost 100% fatal.

Our attempt to control this disease by some form of vaccination proved to be, thus far, of but limited value. The only vaccination that has been tested long enough and was found to give some measure of immunity without risk to the individual, was the B.C.G. vaccine. This vaccine composed of living but avirulent tubercle bacilli, usually does not produce progressive tuberculosis in man and after the incubation period is over, the tuberculin test becomes positive and with it some immunity to tuberculosis develops. The primary B.C.G. complex produced by this vaccine heals completely but the sensitivity to tuberculin is maintained.

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In the control studies on the usefulness of B.C.G. vaccination, as reported by Shirley H. Ferabee,[1] the Deputy Director of Research for the United States Public Health Service, several very interesting facts were re-emphasized. Three groups of individuals were studied. One group was composed of those who reacted positively to tuberculin, apparently as a result of contact with open tuberculosis; a second group of persons who were negative and were held as unvaccinated controls; and a third group was composed of those who were negative reactors to tuberculin but were converted to positive by being vaccinated with B.C.G.

The studies were carried out in widely separate geographic locations representing high and low tuberculosis morbidity and mortality rates and the most interesting finding was that, in all of these locations, most cases of tuberculosis occurred among those who were originally positive reactors to tuberculin.

Thus, in the Puerto Rican control studies, children from one to eighteen years were included. There were 82,000 positive reactors, 27,000 negative reactors, and 50,000 who were tuberculin negative but were converted to positive by being vaccinated with B.C.G. After four years of observation, it was found that there were 577 who developed tuberculosis in the positive reactors, 65 in the vaccinated group, and 53 in the control group. This means that three-fourths of the cases occurred in those who were already tuberculin positive, and who were obviously ineligible for vaccination with B.C.G. It would seem from these figures that our greatest problem is with those who have a positive tuberculin reaction as a result of having been infected after exposure to open cases of tuberculosis. These individuals may harbor within their bodies virulent pathogenic organisms and when, for some reason, the natural resistance of the individual becomes lower, tuberculous disease develops.

The problem then, is what to do with these positive reactors, resulting from exposure to tuberculosis. The answer to this question is not easy. There were, and still are, many workers in tuberculosis who feel that while the primary infection may protect the child against reinfection from exposure to new cases of tuberculosis, there was nothing to be done against the danger of endogenous infection which could occur at any time during the lifetime of the individual.

In the Prendergast[2] Preventorium in Boston, Massachusetts, we tried to show that Preventorium care of school age children infected with tuberculosis and showing a positive tuberculin reaction, ex-

erts a favorable effect in the prevention of occurrence of pulmonary tuberculosis in later life. In a survey by the author of 1390 cases discharged from the Preventorium, over a period of sixteen years, it was found that in 409 children who were supervised over a period of about 13 years, there was an incidence of 2 2/10% who developed pulmonary tuberculosis. This was a very favorable number as compared with the reports of different authors who reported anywhere from 6 4/10% to 15% in similar groups of similar ages and similar social conditions observed over a similar length of time.

Obviously, it would be impractical and too expensive a proposition to treat all positive reactors in Preventoria, especially since we know that in over 88% of these cases the treatment would be useless or at least superfluous. Thus, we at the Boston Tuberculosis Association feel that while Preventorium care is definitely helpful, it is too expensive and not practical.

With the advent of anti-tuberculous chemo-therapy, however, our entire outlook in the problem of tuberculosis has undergone tremendous changes. Complications to mention just a few, such as tuberculous meningitis and miliary tuberculosis previously considered almost hopeless, now have yielded to increasingly effective anti-tuberculosis therapy. This was particularly true after the introduction of isoniazid to our armamentarium as very few cases of tuberculous meningitis developed while a patient was on this drug.

It was Dr. Edith Lincoln who recognized the promise of isoniazid in the prevention of early complications in primary tuberculosis and was largely responsible for a well controlled and cooperative study on its value.

A preliminary report on the prophylactic value of isoniazid in primary tuberculosis in children as obtained by a well controlled and cooperative study of 32 clinical investigators was prepared by Shirley H. Ferabee[3] and others. It was shown that isoniazid was effective in the prevention of about 80% of early complications in primary tuberculosis. This was accomplished by the administration of relatively small doses of isoniazid; 4-6 miligrams per kilo, a dose now considered by many as quite inadequate. When the proper dosage and proper duration of treatment is definitely established, we may expect even more spectacular results.

Since it has been established that isoniazid is effective in the prevention of early post-primary complications, such as miliary tuberculosis and tuberculous meningitis, we are naturally inter-

ested as to its probable role in the prevention of later manifestations such as pulmonary tuberculosis in the adolescent and adult. We know that isoniazid cannot prevent indefinitely infection with a tubercle bacillus in a non-infected person. To do this, as was shown by animal experimentation, we would have to administer the drug indefinitely to maintain an adequate blood level. When, however, an infection with the tubercle bacillus has taken place, and a latent focus has been established, isoniazid may play an important role in prophylaxis in the spread of the disease.

The purpose of isoniazid would not be to eradicate the tuberculous focus, but rather to minimize the danger of the dissemination of the disease from the original focus and at the same time to allow enough organisms to be alive in the lesion to insure the persistence of allergy and real immunity. Thus, by treating the latent tuberculous focus or foci with isoniazid, we may succeed in preserving the allergy and immunity obtained from the primary infection and at the same time reduce greatly the risk of the eventual development of clinical tuberculosis, from these same foci. If we are successful in accomplishing this, we may have in isoniazid a valuable drug which may help to prevent the development of adult type tuberculosis in our positive reactors who cannot enjoy the help from B.C.G.

It is of course, impossible to tell definitely, at the present time, whether isoniazid will be effective in preventing the later complications of primary tuberculosis as it was in the prevention of early ones. We will not have the final answer to this until we have a large number of well controlled cases followed over a long enough period of time to decide whether latent tuberculous foci harboring virulent tubercle bacilli can be treated successfully with isoniazid. We do, however, have some encouraging evidence at the present, both from animal experimentations and clinical observation.

In experiments with guinea pigs, Carroll E. Palmer[4] has noticed that isoniazid exerts a prophylactic effect even after the drug has been discontinued, and that these highly susceptible animals surviving a treated virulent challenge, acquire some degree of resistance to a subsequent untreated virulent challenge. He has shown, furthermore, that if they get a fairly large dose of isoniazid during their first challenge, their protection against a later challenge seems to be less than if they had a smaller but still effective dose. This would indicate that the protection afforded by isoniazid does not depend on the eradication of the original infection but rather on its stabilization.

Clinically, we have noted at the Prendergast Preventorium that nonspecific measures as afforded by Preventorium care, were efficient in reducing the number of cases of pulmonary tuberculosis in later life. Certainly, we may expect the same and even better results by the use of more specific measures such as isoniazid.

A preliminary report by Professor Robert Debré[5] of the work carried out by the French National Institute of Hygiene corroborates the value of the use of isoniazid in children with asymptomatic tuberculous infection. In an eighteen month study of 3000 school children with controls, it was shown that the treatment of children of school age with positive tuberculin reactions, gave very satisfactory results. They all tolerated isoniazid very well and in those cases where the Xrays showed lung opacities, apparently due to tuberculous infection, the opacities cleared much more quickly than in the controls.

Following the lead of Debré, we inaugurated a similar program at the Boston Tuberculosis Association. We picked those children who gave a definitely positive tuberculin reaction and had a history of massive exposure such as familial contagion as contrasted with the socalled "street T. B." where the infection was transient, and of course, those who showed Xray evidence of primary tuberculosis in the lung. These children were given approximately 10 mg. per kilo of isoniazid daily, and PAS 200 mg. per kilo to protect against possible development of isoniazid resistance.

Up to the present, the numbers treated are too few and the length of time too short to warrant any conclusions. However, our results were similar to the ones reported by Professor Debré. Those who showed Xray evidence of infection, showed a marked reduction in the Xray shadows, and isoniazid also seemed to have a definite effect in some cases, on the reduction of the intensity of the tuberculin reaction.

SUMMARY

In summarizing, the following points deserve to be emphasized:

1. Most cases of active tuberculosis occur in the tuberculin positive group.

2. Preventorium care of these children consisting mainly of nonspecific measures, such as good food, proper rest, fresh air and good medical supervision as shown in the study at the Prendergast Preventorium, proved to be beneficial in the prevention of adult type tuberculosis, but because of the large numbers involved and

the expense that it would incur, it was found to be impractical.

3. Isoniazid was found to be highly effective on the prophylaxis of early complications of primary tuberculosis during the period of its administration.

4. Animal experimentations has shown that a certain degree of resistance or immunity to tuberculosis persists after the cessation of the administration of the proper doses of isoniazid.

5. In view of the low toxicity of isoniazid and the minimal expense involved, the role of isoniazid as an aid in the prevention of tuberculosis when used in the treatment of primary tuberculosis deserves further exploration.

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416 *Marlborough Street, Boston* 15

PRELIMINARY INSTITUTIONAL EVALUATION OF A NEW DRUG IN CEREBRAL PALSY

N-Isopropyl-2-Methyl-2-Propyl-1, 3 Propanediol Dicarbamate (Soma*)

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Maryland

Effective institutional evaluation of any new drug to aid in the treatment of cerebral palsy requires not only the long-term testing needed for any chemical agent in any condition but, in addition, minute consideration of many different reactions in each individual patient affected. Preliminary testing must determine objectively the drug's effect on large and small muscles and subjectively, its effect on the patient's sense of well-being. When this phase of evaluation is completed, the drug must then be further investigated, if it proves of value, for specific therapeutic application and effect in various types of patients, with recording of its effects concentrated on the areas selected for intensive—uncontrolled—study.

At the Children's Rehabilitation Institute for Cerebral Palsy, a drug is evaluated on the basis of its place in the Institute's routine, intensive therapy program. The drug is considered successful insofar as it helps the patient to accept highly organized therapy, particularly physical therapy, the most important therapeutic department for any group with few skills. Independence and control of motion encouraged by physical therapy is the first requirement for rehabilitation of the patient and the basis for further independence acquired by training in other modalities of occupational therapy and speech.

Evaluation stresses objective indications of improvement as shown chiefly by changes in the patient's achievements in activities that can be graphed. Subjective indications, such as observations of therapists and parents, are also important and are considered in rating the patient, but final judgment is more dependent on objective results.

USE OF DRUGS IN CEREBRAL PALSY

Several drugs have been in common use for specific conditions in cerebral palsy. Neostigmine, once highly publicized to have

* Soma, supplied by Wallace Laboratories, New Brunswick, New Jersey.
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wide application in cerebral palsy, was found to relax only the smaller muscles and is now given to certain patients with rigidity, to help them in speech therapy and in occupational therapy requiring use of the hands. Paralytic drugs, such as curare and its derivatives, may eliminate partially the necessary motions in athetoid patients and the spasticity in spastic patients during the two-to-three hour period of their effectiveness. In cases where epilepsy is part of of the syndrome, or where the patient is tensed severely, anticonvulsants may be indicated. Excitement in athetoid patients is sometimes relieved by using sedatives such as phenobarbital.

Tranquilizing drugs used for both physical and mental relaxation in patients with cerebral palsy are rauwolfia and its derivatives and meprobamate. These physical-mental relaxants constitute an entirely new field of drug therapy in cerebral palsy—an area of investigation of interest to the neurologist and psychiatrist as well as to the orthopedist and pharmacologist.

The drug that is the subject of this study is N-isopropyl-2-methyl-2-propyl-1, 3 propanediol dicarbamate (Soma). It is a new meprobamate derivative having stronger muscle-relaxant properties than meprobamate and little tranquilizing effect.

Preliminary evaluation of the drug was made with 42 patients of the Children's Rehabilitation Institute, Inc., for Cerebral Palsy. Ages ranged from 4 to 14 years, and diagnoses covered four broad classifications of cerebral palsy as follows: spasticity, mainly spastic quadriplegia, 17 patients; athetosis, rotary and dystonic, 14 patients; rigidity, intermittent, 9 patients; and ataxia, 2 patients. Degree of severity was diagnosed as moderate in 19, severe in 15 and mild in 8. Of the 42 patients, only 3 could walk, feed, and type independently; 2 could dress themselves; and 12 could talk intelligibly. Almost half the group was speechless. Etiology of the conditions varied, the most common causes being the Rh factor, anoxia, premature birth, birth injury, and developmental defects. Other causes were postencephalitis, postjaundice (not Rh) at three days of age, postinfectious influenza at five weeks of age, petechial hemorrhage and anoxia, hypoxia, pressure change at birth, asphyxia at birth, intracranial hemorrhage at birth, and congenital or developmental defects.

Pharmacological studies had shown that the acute and chronic toxicity of the drug was exceptionally low. In human beings no effects on respiration, blood pressure, blood counts, or chemistry had been encountered, nor was renal, hepatic, or endocrine function affected.

METHOD OF STUDY

The test period for patients using the new agent was divided into three parts: an "on" period of 29 days, an "off" period of 28 days, and a final "on" period of 76 days. Patients' reactions were followed for the entire period of 133 days, and reactions of the "off" period were considered as important as those during the "on" periods. The patients were not receiving other drugs except for routine vitamins and an occasional laxative or aspirin tablet if they had a cold.

Dosage was constant: one 250 mg. capsule at breakfast and dinner, with a glass of water or milk. (After the 29 day period, the duration of effect of the drug was determined to be about six hours, and the second dose was shifted to 2 p.m. to gain full advantage of the drug for afternoon therapy).

SIDE-EFFECTS

No adverse effects were noted with use of Soma. No toxicity was apparent, and appetite and bowel habits remained normal in all patients.

No behavioral changes were noted in 32 of the 42 patients in the test. Sole behavioral changes that could be classified as side-effects were occasional lethargy and drowsiness, or a tendency to sleep more than usual in 10 patients. These slight reactions occurred in patients aged 5 to 12 years and in all four classifications of cerebral palsy. No patients were removed from the test because of side-effects.

RECORDS AND RESULTS

Three types of records were kept during the 133-day test: (1) day-to-day tally sheets (subjective ratings by therapists) in four therapeutic departments; physical therapy, occupational therapy, speech, and school; (2) graphs (objective ratings) of changes in performance of therapeutic activities in three departments: physical therapy, occupational therapy, and speech; and (3) key cards (summary of (1) and (2) of each patient) which formed an index for evaluation.

Day-to-Day Tally Sheets. Therapists in each of the four departments recorded a daily report for each patient. (It was not possible to report every day in all departments for all patients—hence the discrepancy in totals.) Patients received a "better" grade only if the final "plus" score of daily tests was higher than the final "no

change" score. In some cases, patients with "plus" scores only slightly lower than "no change" scores received a "better" grade also, but only if the objective results from their performance graphs were high. In all other cases, patients received a "no change" grade even if their day-to-day tally sheets showed "plus" scores almost as high as their "no change" scores.

Day-to-Day Scores of Tally Sheets

(Subjective Ratings)

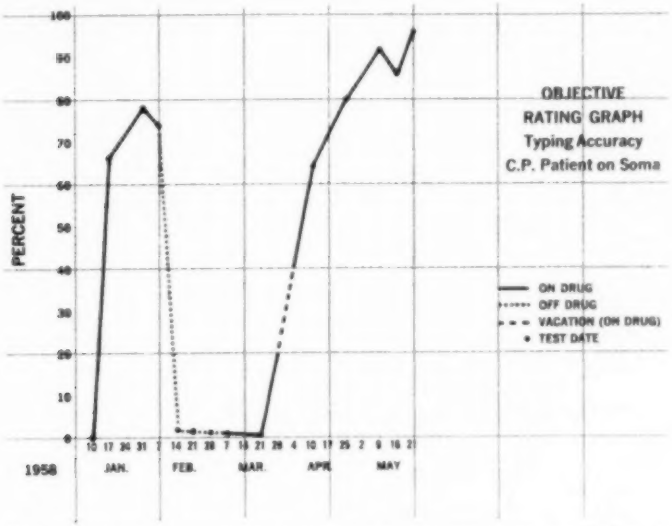
TABLE I

Department	Total No. Pt. Rated	No Change	Better	% Improved
Physical Therapy				
Spasticity	17	13	4	23
Athetosis	14	9	5	35
Rigidity	9	5	4	44
Ataxia	2	2	0	0
Total	42	29	13	30
Occupational Therapy				
Spasticity	16	16	0	0
Athetosis	14	12	2	14
Rigidity	9	9	0	0
Ataxia	2	2	0	0
Total	41	39	2	4
Speech				
Spasticity	8	5	3	37
Athetosis	13	13	0	0
Rigidity	7	4	3	43
Ataxia	2	2	0	0
Total	30	24	6	20
School				
Spasticity	14	11	3	21
Athetosis	12	6	6	50
Rigidity	7	5	2	28
Ataxia	2	1	1	50
Total	35	23	12	34

It will be noted (table I) that the athetoid group showed improvement in subjective rating in physical therapy (5 of 14), occupational therapy (2 of 14) and school (6 patients out of 12). While spastic patients did not score so highly in the day-to-day tally sheets in physical therapy, their improvement in the graph (objective) results (table II) rated them the highest in final evaluation. Spastic patients and those with rigidity were the only ones

to score in speech, but the percentage of their improvement in school was not high as in the athetoid group.

Group results in Therapeutic Activities. Throughout the 133-day test, graphs were kept for each patient in all therapeutic departments except school. Activities were graphed to show the progress of each patient on a scale starting at 0 for no change, and running +1 through +5 for improvement and –1 through –5 for deterioration. The graphs were charted against a ("time required") and



The typical graph shown here indicates the improvement in one patient in one specific performance area—per cent of typing response to flash cards. The graph covers a five-month period during which the patient was tested 14 times, both on and off the drug. In this instance the drug was discontinued May 19, 1958 and the response considered satisfactory.

("number completed") base for repetition of independent acts for any other activities or modalities that would permit comparison and indicate improvement or deterioration. (See graph) It was not possible to carry out tests in each department for all patients, due to illness or lack of previous therapy to prepare the patients for the tests. Also, in some cases, graphs were incomplete and hence not considered in the evaluation. Some patients were graphed in more than one activity in a department. Improvement in one of the activities graphed is shown as improvement in table II.

Graph ratings were not only considerably higher than tally sheet ratings but also showed different results according to classification of the patients' conditions (table III). In physical therapy

improvements was recorded in 25 of 41 tests, and in occupational therapy improvement was recorded in 12 out of 28 tests (table II). These results are in contrast with the therapists' subjective reports of less than one-third improvement in physical therapy and only 4% improvement in occupational therapy (table I). Fifteen of the patients graphed, or over half, improved in speech, while only one-fifth rated improvement in the daily reports of the therapists.

Performance Graph Results

TABLE II

(Objective Ratings)

Department	Total No. Pt. Graphed	No Change	Better	Worse	% Improved
Physical Therapy					
Spasticity	16	2	14	0	87
Athetosis	14	9	5	0	35
Rigidity	9	2	6	1	67
Ataxia	2	0	0	2	0
Total	41	13	25	3	60
Occupational Therapy					
Spasticity	7	4	3	0	43
Athetosis	12	7	3	2	25
Rigidity	7	0	5	2	71
Ataxia	2	1	1	0	50
Total	28	12	12	4	43
Speech					
Spasticity	7	3	4	0	57
Athetosis	12	6	6	0	50
Rigidity	6	2	4	0	66
Ataxia	1	0	1	0	100
Total	26	11	15	0	57

It will be noted that the graph results show that seven-eighths of the spastic group and two-thirds of the group with rigidity improved in physical therapy while taking the drug. Athetoid patients showed 35% improvement, while the two patients with ataxia seemed worse from over relaxation.

In occupational therapy, spastic patients and rigidity patients averaged more improvement than athetoid patients. Improvement in speech appeared about equal for all patients on the graphs, even though in the tally sheet reports spastic patients and those with rigidity were the only ones to score.

Final Evaluation. Results of the 133-day test were taken from the day-to-day tally sheets and from the departmental graphs and entered on key cards, one for each patient. These key cards served

as an index for highly detailed and varied studies of all types of ratings in each type of patient.

Final evaluation of the new drug was made from the results of the graphs, tally sheets, and from the case histories, also briefed

Comparison of Subjective and Objective Ratings

(Percentage of Patients Improved)

TABLE III

Department	Spasticity		Athetosis		Rigidity		Ataxia	
	Subj.	Obj.	Subj.	Obj.	Subj.	Obj.	Subj.	Obj.
Physical Therapy	23	87	35	35	44	67	0	0
Occupational Therapy	0	43	14	25	0	71	0	50
Speech	37	57	0	50	43	66	0	100
School	21		50		28		50	

on the key cards. The objective rating in physical therapy was the basis for the final grade, with subjective results having supplemental value in grading the "whole" patient. In the final evaluation (table IV), no patient was rated as improved unless he showed improvement in departmental graph rating. Most patients rated as improved to some degree showed gains in both the graph and tally sheet ratings.

In the final analysis, 57% of the 42 patients tested showed benefit in therapy while the drug was being administered. Spastic

TABLE IV

Final Ratings: Degree of Improvement Shown by Graph Ratings (Objective) plus Day-to-Day Tally Sheets (Subjective)

Classification	Total No. Pts.	Improvement				
		Slight	Moderate	Definite	No Change	% Improved
Spasticity	17	5	9	1	2	87
Rigidity	9	3	2	0	4	55
Athetosis	14	4	0	0	10	28
Ataxia	2	0	0	0	2	0
Total	42	12	11	1	18	57

patients improved by 88%; patients with rigidity by 55%; athetoid patients by 28%; and ataxic patients showed no gain.

In general, athetoid patients either scored on the subjective rating and showed no improvement on the graph, or improved slightly on the graph and not on the scores of the day-to-day tally sheets. Improvement in both ratings was rare in the same patient; hence the relatively poor score of this group in table IV.

SUMMARY AND CONCLUSIONS

A preliminary evaluation of N-isopropyl-2methyl-2-propyl-1, 3 propanediol dicarbamate (Soma) in treatment of cerebral palsy was made during a period of 133 days with 42 patients of the Children's Rehabilitation Institute for Cerebral Palsy.

Improvement in spastic patients and those with rigidity was substantially greater than in athetoid patients. Eighty-eight per cent of the spastic patients and 55 per cent of those with rigidity had far better relaxation of the extremities. Braces could be tolerated comfortably for a longer period of time and ability to accept physical therapy was improved.

Although 28 per cent of the athetoid patients improved slightly in their ability to accept therapy, the benefit may have been a subjective one. These patients improved physchologically and were less tense, but they were not helped in control of athetoid motions.

On constant dosage of 250 mg. twice a day, 57% of the patients were benefited in ability to accept therapy during the six hour period of drug effectiveness. Degree of improvement varied between slight and moderate.

In two patients a specific subjective report of easier management was received. One patient with rigidity, became easier to brace and the other, an athetoid patient, was more responsive and happier about being put in his chair.

Dosage had to be kept to the level required to relax the contractures and not increased to the point where it caused weakness.

The drug had no adverse effects, and side-effects were limited to occasional lethargy or drowsiness.

Results indicate that Soma is a safe and useful aid to therapy in patients with cerebral palsy and appears to be superior to any other drug now available under similar testing situations for the relief of spasticity and rigidity. Further investigation in related fields of abnormal and uncoordinated muscular disorders would be of value. Of particular interest would be additional data relating the drug's usefulness in the management of such disorders in the physician's office and in the home, as its freedom from serious side-effects and relative ease of administration would appear to make it suitable for this application.

Note: This "Evaluation" by Dr. Phelps will be followed in July Archives by an "Outpatient Study" by Doctors Catherine E. Spears and Winthrop Morgan Phelps.

3038 *St. Paul Street, Baltimore, Maryland*

A CASE OF CONGENITAL AMEGAKARYOCYTIC THROMBOCYTOPENIA WITH LEUKEMOID BLOOD PICTURE AND CONGENITAL DEFORMITIES

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The purpose of this communication is to describe a case of fatal hemorrhagic disease in a newborn female characterized primarily by absence of negakaryocytes in the bone marrow, a leukemoid blood picture, and absent radii and ulnae.

CASE HISTORY

A 7½ pound female infant was born on 9/13/57 to a 28 year old white female and a 40 year old "negroid" father. Congenital deformities of the upper extremities were obvious at birth. Because the mother had not received vitamin K prior to delivery, the infant was given 2.5mg. of vitamin K intramuscularly at birth. The day after birth the infant coughed and vomited bloody mucus. At this time the hemoglobin was 17.1 grams per cent with a hematocrit of 54 per cent. The white blood count was 39,400 with 6 metamyelocytes, 10 band forms, 62 segmented neutrophils, 2 basophils, 5 eosinophils, 7 lymphocytes and 8 nucleated red blood cells. The serology was negative, and the prothrombin time was 80 per cent of the normal control. The infant was given 50mg. of ascorbic acid.

On the fourth day of life there was rather profuse bright red vaginal bleeding, at which time the infant had a hemoglobin of 13.6 grams per cent and a hematocrit of 45 per cent. The white blood count was 141,000 with 13 myelocytes, 4 metamyelocytes, 3 band forms, 54 segmented neutrophils, 2 basophils, 1 eosinophil, 22 lymphocytes and 2 monocyte. The peripheral smear showed marked anisocytosis and poikilocytosis. The platelet count was 18,000 at this time.

A tibial bone marrow showed a marked increase in overall cellularity without megakaryocytes identified in the smears examined. There was a marked increase in the granulocytic series with the predominant cell being progranulocytes. There was also an increased number of blast forms. The erythroid series showed very few early forms with most cells being metarubracytes. The myeloid to erythroid ratio was greater than 10 to 1. The peripheral smear

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and bone marrow were interpreted as being compatible with subacute granulocytic leukemia.

The picture of erythroid hypoplasia brought up the question of Fanconi's hypoplastic anemia. The patient continued to bleed from venipunctures and heel sticks and required several transfusions. The infant was placed on steroids with marked improvement for 14 days but thereafter continued to bleed into the skin, eyes, umbilical cord and vagina. Until the patient's demise at the age of one month, she continued to show marked anemia, thrombocytopenia, and increased number of peripheral white blood cells with marked immaturity of the neutrophilic granulocytes, except the day prior to death when the white blood cell count was 4900. The mode of death was cardiac failure due to severe anemia with edema, hydrothorax, and hydropericardium.

At necropsy the body was that of a female infant of average nutrition and one month's maturity. There were multiple ecchymotic areas about the heels, femoral triangles, eyes and skin of the abdomen. Both radii were absent, but all 5 fingers were present with flexion contracture deformities. There were scattered petechiae in all organs but no evidence of leukemic infiltrate. The sternal and vertebral bone marrow was as previously described.

DISCUSSION

An excellent review of this problem has been published by Emery, *et.al.*,[1] and need not be explored further. Similar cases have been described by Greenwald and Sherman,[2] Landol,[3] Akerren and Reinand,[4] Bernhard, *et. al.*,[5] and Bell, *et.al.*[6] This would be the eighth case of a hypoplastic anemia with amegakaryocytic thrombocytopenia associated with congenital anomalies, namely absent radii and ulnae and a leukemoid blood picture. It is difficult to state whether this represents a case of congenital granulocytic leukemia or Fanconi's hypoplastic anemia, but it would seem that this is probably a variant of Fanconi's anemia.

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Doctor's Building, Omaha 31.

... Authors' Summaries

edited by

MICHAEL A. BRESCIA, M.D.

FERRIS, B. G., JR., MCNICHOL, B. AND SUTIN, G.: THROMBOPHLEBITIS IN PATIENTS WITH SEVERE POLIOMYELITIS. (New England Journal Medicine 259:971 Nov. 13, 1958).

Thrombophlebitis occurred during convalescence in the lower limbs of 9 severely paralyzed patients out of 98 patients who were admitted to a respirator unit, giving a prevalence of approximately 9%.

Thrombophlebitis occurred most frequently in the left lower limb, once bilaterally and once in the right lower limb only. It usually developed within the first six weeks of the illness.

It is suggested that circulatory stasis and hemoconcentration of even mild degree are important in the development of this complication. Dehydration, hypoventilation and possibly other factors are implicated, and hence adequate hydration and ventilation should be maintained during the acute illness.

CHANOCK, R.M., VARGOSKO, A., LUCKEY, A., COOK, M.K., KAPIKIAN, A.Z., REICHELDERFER, T., PARROTT, R.H.: Association of Hemadsorption Viruses with Respiratory Illness in Childhood. (Journal American Medical Association 169:548 Feb. 7, 1959).

In a study involving 1,738 children who were patients in three Washington, D. C., hospitals, types 1 and 2 hemodsorption viruses were recovered almost exclusively from patients with respiratory disease. The results suggest that these agents play an etiological role in respiratory illness. The patients from whom the agents were recovered had illnesses ranging from mild afebrile upper respiratory disease to the syndromes of pneumonia or croup.

The virus recovery rate among patients with respiratory disease was 2.3% for type 1 and 3.9% for type 2. The amount of illness associated with these agents was higher (19.5%) when estimated by the complement-fixation technique. The highest rate of virus recovery (16.7%) or complement-fixing antibody rise (30.2%) occurred for type 2 virus in patients with the croup syndrome.

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*Livingston, S., and Petersen, D.: New England J. Med. *254*:327 (Feb. 16) 1956.

Literature on request.

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